IMMUNOLOGICAL DISTINCTIONS OF ENCEPHALITIS AND POLIOMYELITIS.

BY HAROLD L. AMOSS, M.D.

(From the Laboratories of The Rockefeller Institute for Medical Research.)

(Received for publication, August 26, 1920.)

In the course of the many discussions of encephalitis lethargica which have followed the pandemic of that unusual disease, the question of its relation to epidemic poliomyelitis has been raised either incidentally or directly. Von Economo,1 who reported the first Austrian cases, believed that poliomyelitis could be excluded, while Draper,2 who studied the residual pareses in some of the cases in the English outbreak of 1918, concluded that many of them were true cases of poliomyelitis; however, he called attention to certain phenomena distinctly unusual in experiences with poliomyelitis and left open the question as to whether in the whole group there existed a subsection representing a new disease. Crookshank,3 in discussing the epidemiology, has expressed the view that poliomyelitis, lethargic encephalitis, and possibly still other paralytic epidemic affections, may be different manifestations of one etiologically simple malady.

There are grave objections to the confusion of the etiology of poliomyelitis and lethargic encephalitis. The divergent clinical manifestations have been more marked as the epidemic outbreak of lethargic encephalitis has endured and become more widely distributed. The great difference in the communicability of this affection as compared with poliomyelitis is another point of capital distinction. Apparently the seasonal variation in the prevalence, namely the occurrence of poliomyelitis in the summer and autumn months and

---

ENCEPHALITIS AND POLIOMYELITIS

of lethargic encephalitis in the winter and spring months is no longer so sharp. Netter has reported summer cases of the latter malady in Paris. Moreover, from information furnished by the Department of Health of the City of New York and the statistics in the Public Health Reports of the United States Public Health Service it appears that a similar extension of the period of prevalence is occurring in the United States.

There is one means of distinguishing epidemic poliomyelitis and lethargic encephalitis which has not yet been applied. It relates to the point whether the serum of convalescent cases of lethargic encephalitis can neutralize the virus of poliomyelitis. This fact is readily determined experimentally by the method described by Amoss and Eberson. The principle of the test lies in the power of a neutralizing serum, when administered intraspinally, to prevent the development of poliomyelitis in the monkey following the intravenous injection of a large dose of the virus.

EXPERIMENTAL.

The blood serum of four cases of lethargic encephalitis was used in the test, one from a patient convalescent in the 5th week of the disease, the second in the 4th month, the third in the 5th month, and the fourth 15 months after the attack. The tests were controlled by two experiments in which the same procedure was followed, except that one monkey received intraspinal injections of normal human serum and the other intraspinal injections of poliomyelitic serum from a monkey which had had experimental poliomyelitis 9 months before and recovered with residual paralyses.

The virus of poliomyelitis used came from a strain which had been passed from monkey to monkey many times during the past 9 years and which, between passages, had been preserved in 50 per cent glycerol in the ice box. Before starting the tests this virus was passed through three normal monkeys in order to determine its virulence. The certain infecting dose for intracerebral injection...

6 All intracerebral inoculations were made under ether anesthesia.
was found to be 0.25 cc. of a Berkefeld filtrate of a 5 per cent suspension of the nervous tissues containing the virus.

The infecting power of the virus when given intravenously is shown in the following preliminary experiment.

A monkey received at 5 p.m. an intraspinal injection of 2 cc. of normal horse serum. The following morning 50 cc. of a 5 per cent suspension of fresh virus were given intravenously. 5 days later the animal was weak in both legs and excited. Both arms were paralyzed on the 6th day and the monkey died on the 7th day.

Autopsy.—Microscopic lesions of experimental poliomyelitis were found.

In making suspensions for intravenous injections the tissues used must be fresh. Accordingly, a monkey prostrate from an intracerebral injection of 0.5 cc. of a suspension of the virus 6 days before, was killed with ether and autopsied at once. A 5 per cent suspension of the cord and medulla was prepared for immediate injection.

**Series 1.**

**Experiment 1.—Macacus rhesus A.** Normal human serum control. Mar. 11, 1920, 5.50 p.m. Injected intraspinally 2 cc. of fresh normal human serum. Mar. 12, 2.30 p.m. Injected intravenously 50 cc. of a 5 per cent suspension of fresh poliomyelitis nervous tissue. 2.50 p.m. Intraspinal injection of 2 cc. of fresh normal human serum. The intraspinal injection of 2 cc. of normal human serum was repeated daily for 3 days. Mar. 18. Excited; slight head tremor and left facial paralysis. Mar. 19. Prostrate. Mar. 20. Etherized when moribund.

Autopsy.—Microscopic lesions of experimental poliomyelitis.

**Experiment 2.—Macacus rhesus B.** Immune poliomyelitic serum. Mar. 11, 1920, 6 p.m. Injected intraspinally 2 cc. of serum from a monkey which had had experimental poliomyelitis 9 months before and had recovered with residual paralyses. Mar. 12, 3 p.m. Injected intravenously 50 cc. of virus suspension. 3.25 p.m. Intraspinal injection of 2 cc. of poliomyelitic immune monkey serum. The intraspinal injections of 2 cc. of immune monkey serum were repeated daily for 3 days. The monkey remained well.

**Experiment 3.—Macacus rhesus C.** Serum from convalescent case of lethargic encephalitis. Mar. 11, 1920, 6.05 p.m. Injected intraspinally 2 cc. of serum from Case 1, age 31 years, who was in the 5th week of well defined lethargic encephalitis with general disturbance of the functions of the central nervous system and involvement of third and seventh cranial nerves. Mar. 12, 3.30 p.m. Intravenous injection of 50 cc. of virus suspension. 3.55 p.m. Intraspinal injection
of 2 cc. of encephalitis serum from Case 1. The intraspinal injection of the encephalitic serum was repeated daily for 3 days. Mar. 17. Animal slow and weak. Mar. 18. Found dead at 9 a.m.

*Autopsy.*—Microscopic lesions of experimental poliomyelitis.

**Experiment 4.** *Macacus rhesus D.* Serum from convalescent case of lethargic encephalitis. Mar. 11, 1920, 6.10 p.m. Injected intraspinaly 2 cc. of serum from Case 2, age 34 years, 3 months after definite attack of lethargic encephalitis in which there was general disturbance of the function of the central nervous system, involving the third and seventh cranial nerves and spinal motor roots. Mar. 12, 4 p.m. Intravenous injection of 50 cc. of virus suspension. 5 p.m. Injected intraspinaly 2 cc. of convalescent encephalitis serum from Case 2. The intraspinal injection of 2 cc. of encephalitic serum was repeated daily for 3 days. Mar. 18. Excited and ataxic. Mar. 19. Prostrate. Mar. 20. Etherized when moribund.

*Autopsy.*—Microscopic lesions of experimental poliomyelitis.

**Series 2.**

The second series of tests carried out at a different time was controlled by an experiment in which normal human serum was used for the intraspinal injections as in Experiment 1. The procedure in this series was the same as in Series 1, except that normal horse serum was used for the preparatory intraspinal injection given the day before the intravenous injection of virus. The same strain of virus employed in Series 1 was again tested for infecting power and used in this series.

**Experiment 5.** *Macacus rhesus E.* Normal human serum control. May 18, 1920, 4.10 p.m. Injected intraspinaly 2 cc. of normal horse serum. May 19, 12 m. Intravenous injection of 50 cc. of virus suspension. 12.25 p.m. Injected intraspinaly 2 cc. of normal human serum. The intraspinal injection of normal human serum was repeated daily for 3 days. May 23. Monkey excited; both legs weak. May 24. Complete paralysis of both legs and right facial paralysis. May 25. Died.

*Autopsy.*—Microscopic lesions of experimental poliomyelitis.

**Experiment 6.** *Macacus rhesus F.* Serum from case of lethargic encephalitis. May 18, 1920, 4 p.m. Injected intraspinaly 2 cc. of normal horse serum. May 19, 11.30 a.m. Intravenous injection of 50 cc. of virus suspension. 11.55 a.m. Intraspinal injection of 2 cc. of serum from Case 3, age 28 years, taken 4½ months after acute onset of lethargic encephalitis. The patient's illness began with dizziness, disturbance of vision, vomiting and fever, and he gradually became stuporous. Later paralyses referable to the seventh and spinal nerves appeared. The intraspinal injection into the monkey of the convalescent serum was repeated
CONCLUSIONS.

Lethargic encephalitis is an epidemic disease, the main manifestations of which relate to injury inflicted upon the central nervous system and in particular the basal ganglia of the brain.

Poliomyelitis is an epidemic disease, the main manifestations of which relate to injury inflicted upon the central nervous system and in particular the gray matter of the spinal cord and medulla oblongata.

At the outset of the epidemic of lethargic encephalitis the two diseases tend to prevail at distinct and different seasons of the year, although recently cases of epidemic encephalitis have arisen in the midsummer months. The two maladies therefore are perhaps less distinguished by seasonal prevalence than has been supposed.

They are, however, distinguished by great differences in communicability to monkeys. Epidemic poliomyelitis is readily transmitted through inoculation of the affected central nervous tissues of man to monkeys, while it may still be regarded as doubtful whether lethargic encephalitis has been communicated to monkeys in this manner.

As the experiments reported in this paper show, the two diseases can be distinguished through the power of blood serum under certain circumstances to neutralize the virus of poliomyelitis. The blood serum of convalescent cases of poliomyelitis whether in man or monkey...
possesses this neutralizing power, while the blood serum of recently convalescent cases of epidemic encephalitis is devoid of it.

On the basis of the distinguishing characters described, it is regarded as desirable at the present time to hold epidemic poliomyelitis and epidemic encephalitis as integrally distinct affections. The latter also may be infectious, yet the main lesions of poliomyelitis are present in the spinal cord, and of epidemic encephalitis in the mid-brain.